REMARKS

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Respectfully submitted,

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Production of Novel New Castledisease Virus Strains from cDNAs and Improved Live Attenuated Newcastle Disease Vaccines

The present invention relates to Newcastle disease virus (NDV). In particular, the invention concerns the production of novel NDV strains from cDNAs and the production of improved Newcastle disease vaccines.

Background of the Invention

Newcastle disease virus (NDV) causes a highly contagious and fatal disease affecting all species of birds. Newcastle disease can vary from mild to highly virulent depending upon the virus strain and the host species (1). The virus is a member of the family Paramyxoviridae (2) and contains a single-stranded negative-sense RNA genome.

The genome of NDV is a single strand negative-sense RNA, which has been founded to consist of 15,186 nucleotides (3). The genomic RNA contains six structural genes, which encode at least seven proteins (4,5). Three proteins constitute the nucleocapsid; specifically the nucleoprotein (NP), the phosphoprotein (P), and the large polymerase protein (L). Two proteins form the external envelope spikes, namely the F and HN proteins. The matrix protein (M) forms the inner layer of the virion. The genomic RNA is tightly bound by the NP protein and with the P and L proteins form the functional nucleocapsid within which resides the viral transcriptive and replicative activities. The HN glycoprotein is responsible for attachment of virus to host cell receptors and the F glycoprotein mediates fusion of the viral envelope with the host cell plasma membrane thereby enabling penetration of viral genome into cytoplasm (6). The HN and F proteins are the main targets for the immune response (7, 8). In common with several other Paramyxoviruses, NDV produces a seventh protein (V) of unknown function by editing of the P gene (5, 9).

NDV follows the general scheme of transcription and replication of other nonsegmented negative-strand RNA viruses. The polymerase enters the genome at a promoter in the 3'extragenic leader region and proceeds along the entire length by a sequential stop-start mechanism during which the polymerase remains template bound and is guided by short consensus gene-start (GS) and gene-end (GE) signals. This generates a free leader RNA and six nonoverlapping subgenomic mRNAs. The

-- CROSS REFERENCE TO RELATED APPLICATION

THIS application is a National Stage Entry of International Application No. PCT/US00/06700, filed May 5, 2000, which claims priority from US Provisional Application Serial Nos. 60/132,597, filed May 5, 1999 and 60/127,072, filed December 16, 1999, the entire specification, claims and drawings of each are incorporated herewith by reference. --